UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,599	12/02/2005	Sibaji Sarkar	054339-053012	6524

50607 7590 01/20/2010

RONALD I. EISENSTEIN
100 SUMMER STREET
NIXON PEABODY LLP
BOSTON, MA 02110

EXAMINER	
JAGOE, DONNA A	
ART UNIT	PAPER NUMBER
1619	
MAIL DATE	DELIVERY MODE
01/20/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,599	SARKAR ET AL.	
	Examiner	Art Unit	
	Donna Jagoe	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-26 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments filed November 6, 2009 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 24-26 and 28 are pending in this application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over DePetrillo et al. U.S. Patent Application Publication 2002/0115665 A1 (A4 from IDS dated 2/12/07).

DePetrillo et al. teach administration of calpain inhibitors (HIV protease inhibitors to patients that are exposed to calpain mediated physiological damage (see abstract) such as thrombotic platelet aggregation (paragraph 6). DePetrillo et al. teach Calpain inhibitors are administered after calpain-mediated physiological damage such as myocardial infarction or stroke or angina (paragraph 106) and teach that said damage includes thrombosis or thrombotic platelet aggregation (paragraph 113). DePetrillo et al. does not specifically recite "fibrinolysis" however, the doses administered in the instant case capable of promoting fibrinolysis are from 5 to 1000 mg (paragraph 103) which partially overlaps with the doses recited in the treatment of DePetrillo et al. from 300 to 2400 mg – (see claims 31-32 of the patent). As noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In re Fitzgerald* (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claims drawn to those things to distinguish over prior art. In

such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same. Although DePetrillo et al. do not specifically recite lysis of the thrombosis or thrombotic platelet aggregation, the burden is shifted to Applicant to prove that the calpain-inhibitors of DePetrillo et al. do not promote fibrinolysis.

Claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hisamichi et al. U.S. Patent No. 6,432,963 B1.

Hisamichi et al. teach pyrimidine-5-carboxamide derivatives having Syk tyrosine kinase inhibition activity (column 1, lines 5-8) for treatment of diseases in which platelet agglutination takes part such as thrombosis and the like (column 13, lines 36-38). It does not specifically teach promotion of fibrinolysis, however, the doses administered in the instant case capable of promoting fibrinolysis are from about 0.5 to about 100 mg/kg of body weight per day (paragraph 102). This dose partially overlaps with the doses recited in the treatment of Hisamichi et al. who teaches from about 0.001 to 100 mg/kg (column 16, lines 27-30). As noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In re Fitzgerald* (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claims

drawn to those things to distinguish over prior art. In such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same. Although Hisamichi et al. do not specifically recite lysis of the thrombosis, the burden is shifted to Applicant to prove that the Syk kinase inhibitors of Hisamichi et al. do not promote fibrinolysis.

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over DePetrillo et al. U.S. Patent Application Publication 2002/0115665 A1 and Hisamichi et al. U.S. Patent No. 6,432,963 B1 as applied to claims 24-26 above, and further in view of the legal decision of in re Kerkhoven.

DePetrillo et al. teach administration of calpain inhibitors (HIV protease inhibitors to patients that are exposed to calpain mediated physiological damage (see abstract) such as thrombotic platelet aggregation (paragraph 6). DePetrillo et al. teach Calpain inhibitors are administered after calpain-mediated physiological damage such as myocardial infarction or stroke or angina (paragraph 106) and teach that said damage includes thrombosis or thrombotic platelet aggregation (paragraph 113). Additionally, it teaches administration of another therapeutic agent, such as another calpain inhibitor (paragraph 103). DePetrillo et al. does not specifically recite "fibrinolysis" however, the doses administered in the instant case capable of promoting fibrinolysis are from 5 to

1000 mg (paragraph 103) which partially overlaps with the doses recited in the treatment of DePetrillo et al. from 300 to 2400 mg – (see claims 31-32 of the patent). As noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In re Fitzgerald* (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claims drawn to those things to distinguish over prior art. In such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same. Although DePetrillo et al. do not specifically recite lysis of the thrombosis or thrombotic platelet aggregation, the burden is shifted to Applicant to prove that the calpain-inhibitors of DePetrillo et al. do not promote fibrinolysis.

Hisamichi et al. teach pyrimidine-5-carboxamide derivatives having Syk tyrosine kinase inhibition activity (column 1, lines 5-8) for treatment of diseases in which platelet agglutination takes part such as thrombosis and the like (column 13, lines 36-38). It does not specifically teach promotion of fibrinolysis, however, the doses administered in the instant case capable of promoting fibrinolysis are from about 0.5 to about 100 mg/kg of body weight per day (paragraph 102). This dose partially overlaps with the doses recited in the treatment of Hisamichi et al. who teaches from about 0.001 to 100 mg/kg (column 16, lines 27-30). As noted in *In re Best* (195 USPQ 430 (CCPA 1977)), and *In*

re Fitzgerald (205 USPQ 594 (CCPA 1980)), the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claims drawn to those things to distinguish over prior art. In such a situation, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same. Although Hisamichi et al. do not specifically recite lysis of the thrombosis, the burden is shifted to Applicant to prove that the Syk kinase inhibitors of Hisamichi et al. do not promote fibrinolysis.

Both DePetrillo et al. and Hisamichi et al. teach treatment of diseases in which platelet agglutination takes part such as thrombosis.

As stated in In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980):

It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose. In re Susi, 58 CCPA 1074, 1079-80, 440 F.2d 442, 445, 169 USPQ 423, 426 (1971); In re Crockett, 47 CCPA 1018, 1020-21, 279 F.2d 274, 276-77, 126 USPQ 186, 188 (CCPA 1960). As this court explained in Crockett, the idea of combining them flows logically from their having been individually taught in the prior art.

Thus the claims fail to patentably distinguish over the state of the art as represented by the cited references.

Accordingly, for the above reasons, the claims are deemed properly

rejected and none are allowed.

Response to Arguments

Applicant states that claim 26 has been amended to make explicit that which was implicit, namely, that the method is not being used randomly to any individual and is being used in a patient diagnosed with having a thrombus or at risk of thrombus formation. Further Applicant states that DePetrillo is not directed to such a patient population and further argues that there is a completely different biological phenomena and pathway involved in fibrinolysis for dissolving a thrombus. In response, DePetrillo et al. teach administration of calpain inhibitors to patients that are exposed to calpain mediated physiological damage (see abstract) such as **thrombotic platelet aggregation** (paragraph 6). The Furie et al. reference provided discloses that when a vessel wall is injured, circulating platelets are recruited to the site of the injury where they become a major component of the developing thrombus which culminates in the generation of thrombin and fibrin (see abstract). In the thrombotic platelet aggregation of DePetrillo et al., a thrombus is formed. DePetrillo is drawn to treatment of said thrombus by administration of calpain inhibitors. Although DePetrillo et al. does not specifically recite that the treatment includes dissolving the thrombus, the dose is determined using an enzyme kinetic equation (paragraph 108) (Enzymes dissolve thrombi as suggested by the Rijken et al. reference provided). Further, DePetrillo et al. teach that the compositions can be used in the treatment of a variety of conditions or diseases associated with calpain activation , including conditions or diseases caused by or

mediated by enzymatically active calpains, such as coronary atherosclerosis and restenosis. Post ischemic calpain activation may also be associated with inter alia **thrombosis** or **thrombotic platelet aggregation** (paragraph 113). DePetrillo et al. does not teach treatment of the thrombosis by balloon angiopathy, it teaches treatment of the thrombosis or thrombotic platelet aggregation by administration of calpain inhibitors. As stated supra, the burden is shifted to the applicant to prove that subject matter shown to be in prior art does not possess characteristic relied on where it has reason to believe that functional limitation asserted to be critical for establishing novelty in claimed subject matter may be inherent characteristic of prior art; whether rejection is based on "inherency" under 35 U.S.C. 102, on "prima facie obviousness" under 35 U.S.C. 103, jointly or alternatively, burden of proof is same.

With regard to Hisamichi et al. Applicant asserts that the reference does not teach or suggest a method to promote fibrinolysis or dissolving the clot using Syk inhibitors. In response, Hisamichi et al. teach treatment of diseases in which **platelet agglutination** takes part such as **thrombosis** and the like (column 13, lines 36-38). The Furie et al. reference provided discloses that when a vessel wall is injured, circulating platelets are recruited to the site of the injury where they become a major component of the developing **thrombus** which culminates in the generation of **thrombin and fibrin** (see abstract). Hisamichi et al. teach treatment of said thrombosis by administration of the disclosed Syk inhibitors.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna Jagoe whose telephone number is (571) 272-0576. The examiner can normally be reached on Monday through Friday from 8:00 A.M. - 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler can be reached on (571) 272-0871. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/YVONNE L. EYLER/
Supervisory Patent Examiner, Art Unit 1619

Donna Jagoe /D. J./
Examiner
Art Unit 1619

January 12, 2010